## REMARKS

### I. Status of and Amendments to the Claims

Claims 5, 13, 21 and 22 are canceled. Claims 1, 2, 4, 14-20 and 23 are amended. Claim 24 is added. Claims 1-4, 6-12, 14-20, and 23-24 are pending in the application. The amended and added claim language has support in the specification as originally filed, so that no new matter has been added.

### II. Amendments to Specification

Tables 2 and 3 have been amended to correct an inadvertent typographical error. "R" in the Tables should be "$R_1$". Support for these amendments is found at page 13, line 12, and at page 14, line 2.

The second paragraph on page 16 has also been amended to correct typographical errors. Since the specification inadvertently has two "Tables 4", the first "Table 4" at page 18 and reference thereto at page 17 have been amended to be labeled as "Table 3A."

### III. Priority

The Office Action states that the COOR1 group for substituent R and certain moieties for R1 have support in the parent application 08/857,811. However, remaining moieties for R and most for R1 do not have support, therefore, the claims are treated as having an effective filing date of September 29, 2000. An intervening art rejection may be overcome by cancelling the relevant claim limitations or submitting an affidavit under 1.131.

**Response**

Where R is $-COOR_1$ has been removed from the claims.

### IV. Claim Objections

Claims 2, 4, and 5 were objected to because of informalities regarding the term "which."

**Response**

Claims 2 and 4 have been amended to replace "which" with language that has antecedent support. Claim 5 has been canceled.

### V. Ownership of Claimed Invention

The subject matter of the claims was commonly owned at the time the claimed invention was made.

## VI. Rejections of claims under §103(a)

Claims 1-23 were rejected as unpatentable over Camden 6,077,862. In addition, Claims 1-11, 13, and 21-22 were rejected as unpatentable over Ram *et al.* or Nasr *et al.*

**Response**

**Camden U.S. 6,077,862**

A difference in the '862 patent and the claims at issue is the substituents on the benzimidazole portion of the compounds for the claimed methods.

The Federal Circuit has required that specific support must be found in the prior art that "suggests" or "teaches" the modification necessary to resolve the differences of the prior art with a claimed invention. *In re Grabiak*, 226 USPQ 870 (Fed. Cir. 1985). Applicants submit that no such support for changing the R group of the benzimidazole to any of the claimed R groups is found in the '862 patent. The present specification at page 2, lines 31-34, states that carbendazim metabolizes in the body through the hydroxylation of the benzene ring, primarily in the 5-position. The metabolite is not as active in the treatment of cancer as carbendazim. Nowhere in the '862 patent is there a suggestion that further derivatives are desired, let alone the specific derivatives claimed in the methods of the present invention. Since a teaching or motivation to make the structural and chemical changes to the '862 compounds is missing, the claimed invention as a whole would not have been obvious over the '862 patent within the meaning of §103(a).

Since the invention of the independent claims are believed nonobvious, the invention of the claims dependent thereon are also believed nonobvious. Applicants respectfully request that this rejection be withdrawn as regards the '862 patent.

**Ram et al.**

Claims 13, 21, and 22 are cancelled.

As stated above, specific support must be found in the prior art that "suggests" or "teaches" the modification necessary to resolve the differences of the prior art with a claimed invention. Applicant submits that no such support is found in Ram *et al.*

Ram *et al.* do not teach nor suggest the invention of Claims 1-11 since Ram *et al.* are silent regarding cancers other than leukemia. Ram *et al.* do not teach nor suggest the invention of Claim 24 since Ram *et al.* fail to teach derivatives of methyl 1H-benzimidazole-2-carbamate where the R substituent on the benzimidazole ring is coupled to the ring by an oxygen.

The claimed invention as a whole, therefore, would not have been obvious over Ram *et al.* within the meaning of §103(a). Since the independent claims are believed nonobvious over Ram *et al.*, the

dependent claims are likewise believed nonobvious over Ram *et al.* Applicants respectfully request that this rejection be withdrawn as regards Ram *et al.*

**Nasr *et al.***

Claims 13, 21, and 22 are cancelled.

As stated above, specific support must be found in the prior art that "suggests" or "teaches" the modification necessary to resolve the differences of the prior art with a claimed invention. Applicant submits that no such support is found in Nasr *et al.*

Nasr *et al.* do not teach nor suggest the invention of Claims 1-11 since Nasr *et al.* are silent regarding cancers other than leukemia. Nasr *et al.* do not teach nor suggest the invention of Claim 24 since Nasr *et al.* fail to teach derivatives of methyl 1H-benzimidazole-2-carbamate having an $OCOR_1$ substituent on the benzimidazole ring.

The claimed invention as a whole, therefore, would not have been obvious over Nasr *et al.* within the meaning of §103(a). Since the independent claims are believed nonobvious over Nasr *et al.*, the dependent claims are likewise believed nonobvious over Nasr *et al.* Applicants respectfully request that this rejection be withdrawn as regards Nasr *et al.*

## VII. Obviousness-type Double Patenting

Claim 23 was rejected under the judicially created doctrine of obviousness-type double patenting over Claims 1-15 of U.S. 6,077,862 (Camden).

Claims 1-23 were provisionally rejected under the same doctrine as unpatentable over Claims 1-22 of copending applications 09/676,031 (P&G No. 6643R6), 09/676,409 (P&G No. 6643R4), 09/676,202 (P&G No. 6643R10), and 676,029 (P&G No. 6643R8).

Claims 1-22 were provisionally rejected under the same doctrine as unpatentable over Claims 21-25, 30, and 36 of copending application 08/857,811 (P&G No. 6643).

Claim 23 was provisionally rejected under the same doctrine as unpatentable over Claims 11-20, and 33-37 of 09/552,820 (P&G No. 6643 D3).

**Response**

A terminal disclaimer (Attachment B) is submitted herewith which obviates these rejections. According to the MPEP at section 804.02, the filing of a Terminal Disclaimer simply serves the statutory function of removing the rejection of double patenting, and raises neither a presumption nor estoppel on the merits of the rejection.

In view of the above, it is respectfully requested that the obviousness-type double patenting rejections be withdrawn.

## VIII. Information Disclosure Statement

Provided herewith are copies of all nonpatent art listed in the Form PTO-1449 mailed October 30, 2000 in the present case.

The present application claims priority to copending USSN 08/857,811 (P&G No. 6643). Included herewith are copies of pending applications listed in the Form PTO-1449 mailed October 30, 2000 in the present case that were not provided in the parent application USSN 08/857,811. Copies of the pending applications cited in the 1449 form mailed July 14, 2000, in that parent case, were forwarded on June 22, 2001 to the Examiner for USSN 08/857,811 concurrently with filing a Request for Continued Examination requesting that they be made of record.

Applicants note that the requirement for submission of copies of pending applications did not go into effect until November 7, 2000. Therefore, Applicants are believed not to have been under an obligation to provide copies of pending applications on October 30, 2000 when the IDS was filed.

Applicants respectfully request that the Examiner make the references of the October 30, 2000 Information Disclosure Statement of record.

## X. Conclusion

It is believed that all matters of the Office Action have been addressed. Reconsideration and an early indication of the allowability of the claims are earnestly requested. Should the Examiner have any questions, comments or suggestions that would expedite the prosecution of the present case to allowance, Applicants' undersigned representative earnestly requests a telephone conference at (512) 499-6200.

Respectfully submitted,

Gloria L. Norberg

Date: November 30, 2001

Gloria L. Norberg
Reg. No. 36,706

Akin, Gump, Strauss, Hauer & Feld, L.L.P.
1900 Frost Bank Building
816 Congress Avenue
Austin, Texas 78701
Telephone: (512) 499-6200

## ATTACHMENT A
## VERSION WITH MARKINGS TO SHOW CHANGES MADE

(language to be added is underlined and language to be deleted is enclosed in brackets)

**In the Specification:**

At page 13, Table 2 is amended, as indicated below:

**Table 2**

| Cpd. No. | [R] $\underline{R_1}$ | $R_2$ | LogP |
|---|---|---|---|
| 2-1 | $-CH_2CH_2CH_2N(CH_2CH_3)_2$ | H | 1.098 |
| 2-2 | $-CH_2CH_2$-morpholino | H | 0.018 |
| 2-3 | $-CH(CH_3)CH_2CH_3$ | H | 1.606 |
| 2-4 | $-CH_2$-(2-tetrahydrofuryl) | H | 0.613 |
| 2-5 | $-CH_2CH_2CH(CH_3)_2$ | H | 1.920 |
| 2-6 | $-CH(CH_3)CH_2CH(CH_3)_2$ | H | 2.333 |
| 2-7 | $-CH_2CH_2C(CH_3)_3$ | H | 2.353 |
| 2-8 | $-CH_2CH(CH_3)CH_2CH_3$ | H | 1.992 |
| 2-9 | $-CH\ (CH_2CH_3)_2$ | H | 2.075 |
| 2-10 | $-CH_2CH_2CH_2N(CH_3)_2$ | H | 0.413 |
| 2-11 | $-CH_2CH_2OCH_3$ | H | 0.217 |
| 2-12 | -NH-Ph | H | 1.737 |
| 2-13 | -Ph(2-OH) | H | 1.779 |
| 2-14 | $-CH_2CH_2N(CH_3)_2$ | H | 0.361 |
| 2-15 | $-Ph(3-OCH_3-4-OCH_3-5-OCH_3)$ | H | 1.305 |
| 2-16 | cyclohexyl | $CH_3$ | 2.213 |
| 2-17 | $-CH_2CH_2CH_2CH_3$ | $CH_3$ | 1.836 |
| 2-18 | $-CH_2CH_2CH_3$ | $CH_2CH_2CH_3$ | 2.250 |

At page 14, Table 3 is amended, as indicated below:

**Table 3**

| Cpd. No. | [R] $R_1$ | Log P |
|---|---|---|
| 3-1 | $-CH_2CH_2CH_2CH_2Cl$ | 2.239 |
| 3-2 | $-CH_2CH_2OCH_2CH_2Cl$ | 1.571 |
| 3-3 | $-CH_2CH=CH_2$ | 1.772 |
| 3-4 | $-(CH_2CH_2O)_2CH_2CH_3$ | 1.045 |
| 3-5 | $-CH_2CH_2OCH_2CH_2OH$ | 0.424 |
| 3-6 | $-CH_2CH_2CH=CH_2$ | 2.024 |
| 3-7 | $-CH_2Ph$ | 2.808 |
| 3-8 | $-CH_2CH_2N(CH_3)_2$ | 1.011 |
| 3-9 | $-CH_2CH_2CH_2Cl$ | 1.788 |
| 3-10 | $-CH_2CH=CHCH_2OH$ | 1.121 |
| 3-11 | $-CH_2CH_2CH_2CH_2CH_2OH$ | 1.488 |
| 3-12 | $-CH(CH_2Cl)_2$ | 2.510 |
| 3-13 | $-CH_2CH(CH_3)CH_2C(CH_3)_3$ | 3.802 |
| 3-14 | $-CH_2CF_2CF_3$ | 2.841 |
| 3-15 | $-CH(CH_2F)_2$ | 1.423 |
| 3-16 | $-CH(CH_3)$(cyclopropyl) | 2.155 |
| 3-17 | $-CH_2CH_2F$ | 0.542 |
| 3-18 | $-CH(CH_2Br)_2$ | 2.636 |
| 3-19 | $-CH_2CH(CH_3)CH_2CH_3$ | 2.256 |
| 3-20 | $-CH_2CH_2CH(CH_3)CH_2C(CH_3)_3$ | 4.126 |
| 3-21 | $-CH_2CH_2CH(CH_3)CH_2CH_2CH=C(CH_3)_2$ | 4.048 |

At page 16, the second paragraph is amended as indicated below:

DNA-interactive agents include alkylating agents, *e.g.*, cisplatin, cyclophosphamide, and altretamine; DNA strand-breakage agents, such as bleomycin; intercalating topoisomerase II inhibitors, *e.g.*, dactinomycin and doxorubicin[)]; nonintercalating topoisomerase II inhibitors, such as[,] etoposide and teniposide; and the DNA minor groove binder [plicamydin] plicamycin, for example.

At page 17, the paragraph beginning at line 29 is amended as indicated below:

A listing of currently available chemotherapeutic agents according to class, and including diseases for which the agents are indicated, is provided as Table 3A [4].

At page 18, the title to the table is amended as indicated below:

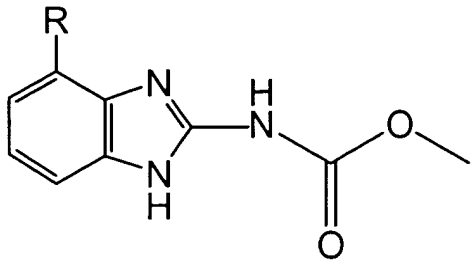
Table 3A [4]. Neoplastic Diseases[1] for which Exemplary Chemotherapeutic agents are Indicated

**In the Claims:**

Cancel Claims 5, 13, 21 and 22.

The following Claims 1, 2, 4, 14-20 and 23 are amended, as indicated below:

1. (Amended) A method for treating [cancer] carcinoma, sarcoma, or lymphoma susceptible to treatment in a warm-blooded animal comprising administering to the warm-blooded animal a therapeutically effective amount of a compound of the following formula **A-1**:



**A-1**

wherein,

R is [–$COOR_1$,] –$CONR_1R_2$, –$OCOR_1$ or –$NHCOR_1$;

$R_1$ is alkyl, haloalkyl, hydroxyalkyl, alkenyl, haloalkenyl, cycloalkyl, cycloalkalkyl, heterocycloalkyl, heterocycloalkalkyl, substituted or unsubstituted phenyl, substituted or unsubstituted phenylamino, substituted or unsubstituted benzyl, alkoxyalkyl, poly(alkoxy)alkyl, hydroxyalkoxyalkyl, hydroxypoly(alkoxy)alkyl, haloalkoxyalkyl, halopoly(alkoxy)alkyl, or aminoalkyl; and

$R_2$ is hydrogen or alkyl.

2. (Amended) A method according to claim 1 [which] wherein the compound is in the form of a pharmaceutically acceptable salt thereof.

4. (Amended) A method according to claim 1 [which] wherein the compound is in the form of a prodrug thereof.

14. (Amended) A method according to claim [1] 12 wherein said [cancer] carcinoma is melanoma.

15. (Amended) A method according to claim [1] 12 wherein said [cancer] carcinoma is colon cancer.

16. (Amended) A method according to claim [1] 12 wherein said [cancer] carcinoma is breast cancer.

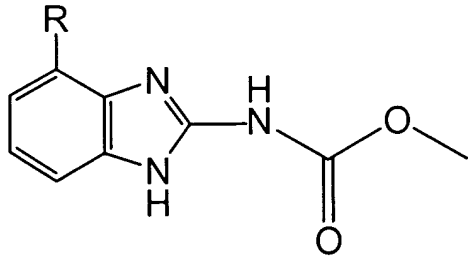
17. (Amended) A method according to claim [1] 12 wherein said [cancer] carcinoma is lung cancer.

18. (Amended) A method according to claim [1] 12 wherein said [cancer] carcinoma is pancreatic cancer.

19. (Amended) A method according to claim [1] 12 wherein said [cancer] carcinoma is ovarian cancer.

20. (Amended) A method according to claim [1] 12 wherein said [cancer] carcinoma is prostate cancer.

23. (Amended) A method for treating a viral infection in a warm-blooded animal comprising administering to the warm-blooded animal a therapeutically effective amount of a compound of the following formula **A-1**:




**A-1**

wherein,

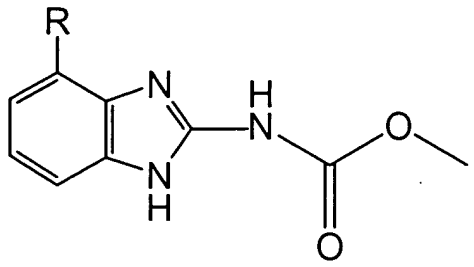
R is [–$COOR_1$,] –$CONR_1R_2$, –$OCOR_1$ or –$NHCOR_1$;

$R_1$ is alkyl, haloalkyl, hydroxyalkyl, alkenyl, haloalkenyl, cycloalkyl, cycloalkalkyl, heterocycloalkyl, heterocycloalkalkyl, substituted or unsubstituted phenyl, substituted or unsubstituted phenylamino, substituted or unsubstituted benzyl, alkoxyalkyl, poly(alkoxy)alkyl, hydroxyalkoxyalkyl, hydroxypoly(alkoxy)alkyl, haloalkoxyalkyl, halopoly(alkoxy)alkyl, or aminoalkyl; and

$R_2$ is hydrogen or alkyl.

Please add Claim 24 as follows.

--24. A method for treating leukemia susceptible to treatment in a warm-blooded animal comprising administering to the warm-blooded animal a therapeutically effective amount of a compound of the following formula **A-1**:




**A-1**

wherein,

R is $-OCOR_1$; and

$R_1$ is alkyl, haloalkyl, hydroxyalkyl, alkenyl, haloalkenyl, cycloalkyl, cycloalkalkyl, heterocycloalkyl, heterocycloalkalkyl, substituted or unsubstituted phenyl, substituted or unsubstituted phenylamino, substituted or unsubstituted benzyl, alkoxyalkyl, poly(alkoxy)alkyl, hydroxyalkoxyalkyl, hydroxypoly(alkoxy)alkyl, haloalkoxyalkyl, halopoly(alkoxy)alkyl, or aminoalkyl.--